REMARKS

Claims 1-55 are currently pending in this application. Claim 47 is withdrawn from consideration. Claims 1-46 and 48-55 stand rejected.

35 U.S.C. §103 Rejections

Claims 1-46 and 48-55 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Impraim, et al. (USPN: 6,228,578) in view of Nathan, et al. (USPN: 6,057,099) and Shah, et al. (USPN: 5,629,156). Applicants respectfully traverse the Examiner's rejection.

The applicants submit that claims 1-46 and 48-55 are patentable over Impraim in view of Nathan, and further in view of Shah. Briefly, the Impraim reference describes a method of detecting a target nucleic acid using RNA probes which hybridize to the target nucleic acid, capturing the hybrid using an antibody specific for the RNA:DNA hybrid, and removing non-hybridized probe by digesting the excess probe with RNase. The Examiner has combined the Impraim reference with Nathan, et al. and Shah, et al. The Examiner admits that Impraim does not "teach blocker probes, immobilization of the probes and use of bridge probes or dT-tailed probes" (Office Action-page 4, ¶5). However, the Examiner contends that it would have been obvious for a skilled artisan to modify the method of detecting a target nucleic acid of Impraim with the step of adding blocker probes as taught by Nathan and dT-tailed probes and immobilization of capture probes as reported by Shah to result in an enhanced and improved method for detecting a nucleic acid target. The applicants, however, respectfully traverse that there is any teaching or motivation to combine the method of detecting a target nucleic acid of

Impraim and the blocker probes of Nathan with the dT-tailed probes and immobilization of capture probes of Shah in order to result in the claimed invention.

Col. 6, lns 34-40 and col. 7, lns. 5-10 of Impraim report that single-stranded HPV RNA probes may be used in screening assays by hybridizing to sample DNA. Impraim does not teach that a capture sequence probe and signal sequence probe both hybridize to the sample nucleic acid. In fact, Impraim only describes one probe type, HPV RNA probes, which hybridize to the sample DNA. Also, Impraim does not teach the use of blocker probes, but rather uses a digestion enzyme such as RNAase which digests and degrades any excess non-hybridized RNA probe. Impraim describes the use of anti-RNA/DNA hybrid antibodies for capturing the hybrid onto the solid phase (Col. 7, lns. 14-22) and further describes detecting the captured hybrid using a direct labeled RNA probe (Col. 9, lns. 63-67).

The Examiner points to col. 5, lns 31-63 of Nathan for teaching the use of blocker oligonucleotides for reducing background signal. However, the blocker probes of Nathan are complementary to the target DNA (Fig. 3; A' or B') as defined in the table at col. 7. In contrast, the blocker probes of the claimed methods are not complementary to the target, but rather contain sequence which is IDENTICAL to the target nucleic acid (see Fig. 2 of the instant specification; A or B) and complementary to the capture sequence probe (CSP). Nathan does not teach or suggest blocker probes because the analogous probe (*i.e.*, the second capture probe) has no affinity for the first capture probes, which is a required function of the blocker probes of the present invention. Thus, Nathan does not teach the blocker probes of the claimed invention

The Examiner contends that Shah teaches "dA-tailed probes (bridge probes) which bind to both target and dT derivitzed supports such that the binding is stronger to the targets than the supports (see column 8, lines 44-54)." Shah further states that the "conditions

can be imposed whereby the probe will separate from the support but not the target." However, the instant invention is directed towards using the bridge probes to enable the detection of the target by "bridging" the target and signal sequence probe. The instant invention utilizes bridge probes to "bridge" the target nucleic acid sequence and the signal sequence probe (SSP) (Figs. 6B-D). The Shah dA-tailed probes capture the target to solid supports, whereas the bridge probes of the present invention enable signal sequence probes to complex with the target already bound to a solid support. Therefore, Shah, as cited by the Examiner, does not teach or suggest bridge probes as claimed.

Thus, Impraim does not teach blocker probes or capture probes. Impraim uses anti-RNA/DNA hybrid antibodies to capture the hybrids to a solid phase. Instead of blocker probes, Impraim uses RNase to remove excess non-hybridized RNA probes. The Nathan and Shah publications do not remedy the deficiencies of Impraim. There is no motivation to use the blocker probes of Nathan with Impraim since RNase is used under conditions sufficient to reduce background noise. Furthermore, the blocker probes of Nathan are not the same as those taught in the instant specification. The bridge probes of Shah serve to capture the target to solid supports. Therefore, none of the references, alone or when viewed in combination, teach or suggest the claimed method as a whole. In reading the cited references, the skilled artisan would not be able to generate the claimed method, which detects double-stranded probe:target nucleic acid hybrids. Thus, applicants respectfully request reconsideration and withdrawal of the §103(a) rejection.

CONCLUSION

Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. 13-4500, Order No. 2629-4017. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 13-4500, Order No. 2629-4017. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

Respectfully submitted,
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